Evaluating antiproliferative drug activity on cells in vitro is a widespread practice in basic biomedical research and drug discovery. Typically, quantitative assessment relies on constructing dose–response curves from 72h end-point assays, for which the de facto standard metric is the number of viable cells 72h after drug addition. Using theoretical modeling and experimentation, we have shown that current metrics of antiproliferative small molecule effect suffer from time-dependent bias, leading to inaccurate assessments of parameters such as drug potency and efficacy [1]. We proposed the drug-induced proliferation (DIP) rate, the slope of the line on a plot of cell population doublings versus time, as an alternative, time-independent metric that eliminates bias due to proliferation rates and drug activity delays [1]. The DIP rate analytical platform incorporates time-lapse cell imaging, automated image processing and cell counting. Single-cell feature acquisition (e.g., division or death) is also available, if desired. These data can be incorporated into mathematical models to predict cellular response dynamics to drug treatment, as well as both genetic and non-genetic perturbations. Both deterministic and stochastic simulations provide an understanding of drug response dynamics at the cell population and single-cell level, respectively. Here we present our approach for scaling the DIP rate platform to a high-throughput screening format capable of obtaining data for approximately 13,000 unique conditions at 12 time points over 5 days. With appropriate, measurable conversion coefficients, it should be possible to translate this information to in vivo experiments and or applications. Thunor, a web-based data management and visualization tool, is also introduced.

[1] L.A. Harris, P.L. Frick, S.P. Garbett, K.N. Hardeman, B.B. Paudel, C.F. Lopez, V. Quaranta and D.R. Tyson, An unbiased metric of antiproliferative drug effect in vitro, Nat Methods. 13 (2016) 497–500. doi:10.1038/nmeth.3852.